OC-0079

Reproducibility of an NTCP model for tube-feeding dependence after H&N radiotherapy

A. van der Schaaf[1], K. Wopken[1], N.M. Sijtsema[1], H.P. Bijl[1], J.A. Langendijk[1], A.A. van 't Veld[1]

[1]University of Groningen University Medical Center Groningen, Radiation Oncology, Groningen, The Netherlands

Purpose/Objective: NTCP models are known to be sensitive to variations in the dataset, leading to high model variability. We tested the reproducibility of a model that we developed for tube-feeding dependence using repeated data-resampling.

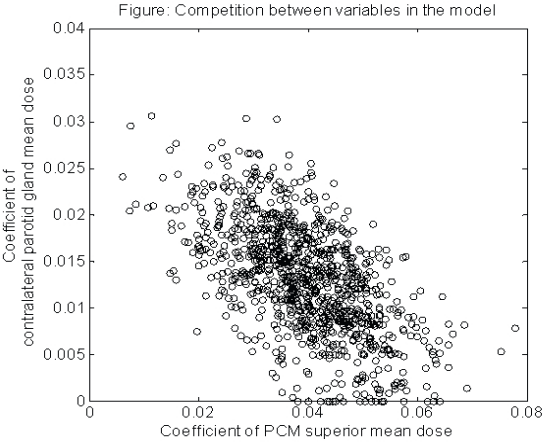
Materials and Methods: A dataset of 416 patients that were treated with H&N radiotherapy in two hospitals was used to fit logistic models, using LASSO penalized learning, to predict tube feeding dependence at six month after treatment. We defined 21 candidate variables (see table), including 13 dosimetric variables. The LASSO method estimated the coefficients of the model, while restricting the coefficients to avoid overfitting. Variables with an estimated coefficient equal to zero were categorized as not selected. To test the reproducibility, we fitted 1000 models in a repeated 10-fold double cross-validation scheme. For each model a different selection of 80% of the original data was used.

Table: Variables in the dataset, ranked by selection frequency.

Rank	Variable	Description	Selection frequency (%)
1	WL	Weight loss prior to treatment (moderate, severe)	100
2	TM	Treatment modality (accelerated, chemoradiation, bioradiation)	100
3	PCMsup	MD to the superior pharyngeal constrictor muscle	100
4	TS	Tumour stage (>2)	100
5	Pc	MD to the contralateral parotid gland	98
6	PCMinf	MD to the inferior pharyngeal constrictor muscle	91
7	CR	Mean does to the cricopharyngeus muscle	90
8	BS	Baseline score for swallowing problems (CTCAE)	85
9	GEN	Gender (male)	77
10	PCMmed	MD to the middle pharyngeal constrictor muscle	56
11	EIM	MD to the esophageal inlet muscle	40
12	AGE	Patient age (>65 year)	31
13	SG	MD to the supraglottis	18
14	Pi	MD to the ipsilateral parotid gland	18
15	NS	Nodal stage (N+)	15
16	SMc	MD to the contralateral submandibular gland	9
17	LAT	Laterality (bilateral treatment)	1
18	SMi	MD to the ipsilateral submandibular gland	1
19	CE	MD to the cervical esophagus	1
20	GL	MD to the glottis	0
21	BT	MD to the base of tongue	0

Results: The prediction performance of the models was good with an average area under the ROC curve of 0.85 in the independent validation sets. The variables 'Weight loss', 'Treatment modality', 'Mean dose (MD) to the PCM superior (PCMsup)', and 'Tumor stage' (see table) were reproducibly identified in all models as strong risk factors. These variables together determine on average 87% of the variance of the linear part of the models. Five variables had a consistently low contribution to the models with selection frequencies below 10%. Eleven variables had an intermediate selection frequency between 100% and 10%. The variable 'MD to the contralateral parotifd gland' (Pc) was selected often (98%), but with a notable negative correlation (-0.58) of the corresponding model coefficient with that of PCMsup (see figure). These two variables have the tendency to compete: when the coefficient of Pc increases the coefficient of PCMsup decreases in the model. This tendency is related to a strong correlation (0.79) of the data of these variables, and it signifies that the effect of both variables in the resulting models is difficult to distinguish from the available data. This behavior is also seen for the variables 'MD to the cricopharyngeus muscle 'and' MD to the esophageal inlet muscle', but much less for other variables, even though the average correlation of the data is relatively high (mean absolute value 0.34). The correlation between model coefficients is mostly close to zero (mean absolute value 0.14).

Figure: Competition between variables in the model



Conclusions: The method of repeated data-resampling enables the assessment of modeling reproducibility and variable competition. The NTCP model for tube feeding dependence is to a large extend reproducible. The four variables with the strongest association with the endpoint are modeled with a high degree of reproducibility, whereas the involvement of 11 variables with weaker associations remains uncertain in various degrees.

OC-0080

Treatment factors impacting on gastrointestinal toxicity following prostate radiotherapy

M. Ebert[1], M. Bulsara[2], A. Haworth[3], R. Kearvell[4], A. Kennedy[4], S. Richardson[4], M. Krawiec[4], N. Stewart[4], D.J. Joseph[4], J.W. Denham[5]

[1]University of Western Australia, Academic Physics, Nedlands WA, Australia

[2]University of Notre Dame, Biostatistics, Fremantle, Australia

[3]Peter MacCallum Cancer Centre, Physical Sciences, Melbourne, Australia

[4]Sir Charles Gairdner Hospital, Radiation Oncology, Perth, Australia

[5]University of Newcastle, Medicine and Population Health, Newcastle, Australia

Purpose/Objective: To assess the impact of treatment planning and delivery technique, as well as patient anatomical factors, on acute and late gastrointestinal toxicity using data from the TROG 03.04 RADAR prostate radiotherapy trial.

Materials and Methods: The RADAR trial accrued 813 external beam radiotherapy participants during 2003-2008. Following review and archive to a query-able database, digital treatment plans and data describing treatment technique for 754 patients were available. Anatomical features including organ volumes, extent and separations were automatically derived from the archived data and exported, together with treatment demographics and results of quality assessment against protocol requirements, for univariate and multivariate regression against toxicity scored using CTC v3.0 criteria and patient-reported quality of life questions at multiple timepoints. Regression analyses were reviewed in the context of dose-volume data for the rectum and anal canal.

Results: With rectal dose-volume constraints applied in the RADAR protocol, toxicity rates have been found to be low. Univariate analysis revealed significant impact of multiple factors on acute and late toxicity, including – patient orientation (prone vs supine); the isodose encompassing the rectum; the number and energy of treatment beams; the number of accruals per contributing centre; the results of dosimetric audits; beam shaping method (blocks/collimators vs MLCs); and dose calculation algorithm. Prostate and rectum dimensions related relatively minimally to toxicity, as did dose conformation indices. Comparison with dose-volume information for the rectum shows that these associations often cannot be explained by variations in planned dose distribution and are likely due to subsequent unrecorded factors (such as setup and organ motion) and confounding associations inherent to the dataset.

Conclusions: Significant interaction has been seen between treatment planning and delivery technique, the quality of radiotherapy planning/delivery and resulting gastrointestinal toxicity for prostate radiotherapy patients. These effects frequently cannot be explained by the underlying planned dosimetry.